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UNITED STATES ENVIRONMENTAL PROTECTION AGENCY

WASHINGTON, D.C. 20460

OFFICE OF
PREVENTION, PESTICIDES
AND TOXIC SUBSTANCES

MEMORANDUM

DATE: 6 NOVEMBER 2008

SUBJECT: FIPRONIL – Exposure/Risk Assessment for the Proposed Experimental Use as a Termiticide Applied in Granular Formulation

PC Code:	129121	DP No.:	358069
MRID No.:	N/A	Registration No.:	
Petition No.:	N/A	Regulatory Action:	Sect. 5
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INTRODUCTION

Under provisions in Section 5 of the Federal Insecticide, Fungicide and Rodenticide Act (FIFRA), as amended, the BASF Corporation has requested an Experimental Use Permit to apply the insecticide active ingredient (ai) fipronil in a granular formulation for termite control.

This memorandum serves as the Agency's assessment of exposure and risk to occupational pesticide handlers (mixers, loaders, applicators). It should be noted that the risk assessment techniques used in this document are those that have been developed and refined by the HED/Office of Pesticide Programs' Science Policy Council for Exposure

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(ExpoSAC). Therefore, the risk assessment methods use herein, are the same as the HED's standard operating procedure (SOP).

USE PATTERN SUMMARY

The use pattern summary is taken from BASF's application for an Experimental Use Permit (EUP).

The product requested for use is not registered and is known as BAS 350 82 I. It is a granular formulation which contains 8.0 % by weight, fipronil a.i. It should be noted that fipronil **is currently registered** by BASF for use as a termiticide in two products; Termidor® SC Termiticide/Insecticide (EPA Reg. No. 7969-209) and Termidor® 80 WG Termiticide/Insecticide (EPA Reg. No. 7969-210).

According to the EUP label, BAS 350 82 I (BAS350) is to be applied "...along the exterior foundation of the structure." BAS350 is to be applied to a trench 6 inches wide and 6 inches deep along the perimeter. The rate of application ranges from 1.87-3.74 ounces/10 linear feet (0.00935-0.0187 lb ai/10 linear feet).

After the correct amount of formulation is applied to the trench, the trench is to be backfilled with soil and a specified amount of water applied to the soil surface.

According to the BASF application, "on average, at each test structure" approximately 300 linear feet will be treated at the various experimental use sites. That equates to 7.0125 lb formulation (per 300 linear feet/site) or 0.561 lb ai per experimental site. The application indicates 120 sites may be treated, thus, 67 lb fipronil ai might be used.

OCCUPATIONAL PESTICIDE HANDLER EXPOSURE

The EUP application states: "All treatments will be applied with BASF authorized equipment or manually according to the BAS 350 82 I EUP label instructions. BASF authorized equipment is specifically designed according to BASF specifications to apply the prescribed amount of BAS 350 82 I and water to the soil in a uniform manner to the prescribed depth of at least 6 inches and not below the foundation footer.... Treatments will be made by a qualified applicator, under the supervision of the EUP Site Contact."

The EUP request did not contain a description or graphics of the specialized BASF application equipment. Therefore, as a "Tier I", conservative, screening model, ARIA/RD will assume that the granules are applied manually.

No chemical specific data were available with which to assess potential exposure to pesticide handlers. The estimates of exposure to pesticide handlers are based upon surrogate study data available in the PHED (v. 1.1, 1998). For pesticide handlers, it is HED standard practice to present estimates of dermal exposure for "baseline" that is, for workers wearing a single layer of work clothing consisting of a long-sleeved shirt, long

pants, shoes plus socks and no protective gloves as well as for "baseline" **and the use of protective gloves** or other PPE as might be necessary.

The EUP labeling states: "All pesticide handlers (mixers, loaders, and applicators) must wear long-sleeved shirt, and long pants, socks, shoes, and chemical resistant gloves. All pesticide handlers must wear a dust/mist filtering respirator (MSHA/NIOSH approval number prefix TC-21C), or a NIOSH approved respirator with any N, R, P or HE filter, when working in a non-ventilated space, including but not limited to crawl spaces and basements. All pesticide handlers must wear protective eyewear (goggles, a faceshield, or safety glasses with front, brow, and temple protection) when working in a non-ventilated space, including but not limited to crawl-spaces and basement, or when applying termiticide by rodding or sub-slab injection."

Please note that the label **specifies** the use of Termidor® SC or Termidor 80 WG for any applications **internal to the structure.** Thus for this assessment, BASF350 is assessed for use ONLY in exterior applications.

The PHED does not contain exposure data specific to the proposed method of application, especially if considering use of the specialized BASF application equipment. ARIA/RD believes that 'manual' application is likely to result in the highest rate of exposure. Therefore, as surrogates, PHED data are used for a Mixer/Loader using Open Pour Loading of Granular formulation and for an individual Applying Granular Bait Dispersed by Hand. The estimates include the use of protective gloves since they are specified in the permit request.

The toxicological factors used in this assessment are taken from: Memo, M. Dow, 18 DECEMBER 2007, "FIPRONIL – Occupational Exposure/Risk Assessment for the Proposed Use of Fipronil to Control Fire Ants in Field Grown Ornamentals", DP Code: 346777.

With regards to the assessment herein, the short-term duration (1-30 days) dermal toxicological endpoint is identified from a 21-day dermal toxicity study in the rat. The effects seen were based on decreased body weight gain and food consumption in both sexes. The No Observable Adverse Effect Level (NOAEL) is 5.0 mg ai/kg bw/day. Since the study was a dermal study, there is no correction for dermal absorption. The level of concern is for Margins of Exposure (MOE) < 100. A 70 kg bw is used to calculate dermal exposure.

The short-term duration inhalation toxicological endpoint was identified from a developmental neurotoxicity study in the rat where the effects seen were decreased group mean pup weights during lactation, and significant increase in time of preputial separation in males. HED and RD assume 100% absorption via the inhalation route of exposure. Since the inhalation toxicological endpoint was identified from a developmental study, a 60 kg bw is used to calculate inhalation exposure.

Although only short-term duration exposures are expected during the course of the proposed study, it should be noted that the intermediate-term dermal and inhalation endpoints are the same as the short-term endpoints. Therefore the estimates of risk for short-term exposures are adequate to describe intermediate-term exposures, in the event that they might occur.

Since the dermal and inhalation toxic effects were identified from different studies and different effects were seen, the Margins of Exposure are combined using the following convention:

$$\text{Combined MOE} = \frac{1}{\frac{1}{MOE_{Dermal}} + \frac{1}{MOE_{Inhalation}}}$$

See Table 1.0 for a summary of estimated exposures and risks to occupational handlers. See the APPENDIX for a summary of toxicological endpoints used for risk assessment.

Table 1.0 Summary of Exposure & Risk to Occupational Handlers From Fipronil

Unit Exposure[1] mg ai/lb handled	Applic. Rate[2] lb ai/unit	Units Treated[3]	Avg. Daily Exposure[4] mg ai/kg bw/day	MOE[5]	Combined MOE[6]
Mixer/Loader - Open Pour Loading Granules					
Dermal: SLWithGlove 0.0069 Inhal. 0.0017	0.0187 lb ai/10 linear ft	300 linear feet/day	Dermal: SLWithGlove 0.000055 Inhal. 0.000016	With Glove 90,909 3,125	3,021
Applicator – Granular Bait Dispersed by Hand					
Dermal: SLWithGlove 0.0020 Inhal. 0.00022	0.0187 lb ai/10 linear ft	300 linear feet/day	Dermal: SLWithGlove 0.000016 Inhal. 0.0000021	With Glove 312,500 23,809	22,123

1. Unit Exposures are taken from "PHED SURROGATE EXPOSURE GUIDE", Estimates of Worker Exposure from The Pesticide Handler Exposure Database Version 1.1, August 1998. SLWithGlove = Single Layer of Work Clothing plus protective gloves; Inhal. = Inhalation. Units = mg a.i./pound of active ingredient handled.
2. Applic. Rate. = Taken from the proposed EUP label
3. Units Treated taken from the EUP application
4. Average Daily Dose (ADD) = Unit Exposure * Applic. Rate * Units Treated ÷ Body Weight (60 kg for inhalation and 70 kg for dermal).
5. MOE = Margin of Exposure = No Observable Adverse Effect Level (NOAEL) ÷ ADD. NOAEL = No Observable Adverse Effect Level (5.0 mg a.i./kg bw/day for short-term dermal and 0.05 mg ai/kg bw/day for inhalation)
6 Combined MOE = $\frac{1}{\frac{1}{MOE_{Dermal}} + \frac{1}{MOE_{Inhalation}}}$

A MOE of 100 is adequate to protect occupational pesticide handlers from exposures to cymoxanil. The estimated MOEs are all > 100. If an applicator were to apply 10x, the MOEs would still by >100. Therefore, the proposed new use does not exceed ARIA/RD's level of concern.

POST-APPLICATION EXPOSURE TO AGRICULTURAL WORKERS

Since the formulation is applied to a trench 6" wide x 6" deep and then covered with backfill and watered in, ARIA/RD believes post-application exposure will be negligible. Thus a post-application exposure assessment is not necessary.

APPENDIX

Acute Toxicity Data on *FIPRONIL*

Guideline No./ Study Type	MRID No.	Results	Toxicity Category
870.1100 Acute oral toxicity -rat	42918628	LD50 = _ 92/_ 103 mg/kg; _+_ 97 mg/kg	II
870.1200 Acute dermal toxicity	42918629 42918630	LD50 = > 2000 mg/kg [rat] = 354 mg/kg [rabbit]	III II
870.1300 Acute inhalation toxicity -rat	43544401	LC50 = _ 0.36/_ 0.42 mg/L; _+_ 0.39 mg/L	II
870.2400 Acute eye irritation -rabbit	42918632	mild transient ocular irritant	III
870.2500 Acute dermal irritation - rabbit	42918633	slight dermal irritant	IV
870.2600 Skin sensitization -Guinea Pig	42918634	non-sensitizing	

Summary of Toxicological Dose and Endpoints for Fipronil for Use in Human Risk Assessment [1].

Exposure Scenario (Fipronil)	Dose Used in Risk Assessment, UF	FQPA SF and Endpoint for Risk Assessment	Study and Toxicological Effects
Acute Dietary all populations including infants and children	NOAEL= 2.5 mg/kg UF = 100 **Acute RfD** = 0.025 mg/kg	FQPA SF = 1 **aPAD** = acute RfD / FQPA SF = 0.025 mg/kg	Acute neurotoxicity - rat LOAEL = 7.0 mg/kg based on: decreased hindleg splay in males at 7 hours.
Chronic Dietary all populations	NOAEL= 0.019 mg/kg/day UF = 100 **Chronic RfD** = 0.0002 mg/kg/day	FQPA SF = 1 **cPAD** = chr RfD / FQPA SF = 0.0002 mg/kg/d	Chronic/carcinogenicity study - rat LOAEL = 0.059 mg/kg/day based on: increased incidence of seizures and death, alterations in clinical chemistry (protein), increased TSH, and decreased T4.
Short-Term Oral (1-7 days) (Residential)	oral study LOAEL ≤0.1 mg/kg/day UF of 3 for no NOAEL, 100 for	**LOC for MOE** = 300 (Residential, includes the FQPA SF)	Developmental toxicity Study - rabbit LOAEL = ≤ 0.1 mg/kg/day based on: maternal toxicity of decreased body weight gain, decreased food consumption, and decreased food efficiency.

	interspecies extrapolation and intraspecies variation		
Intermediate-Term Oral (1 week - several months) (Residential)	oral study LOAEL ≤0.1 mg/kg/day UF of 3 for no NOAEL, 100 for interspecies extrapolation and intraspecies variation	**LOC for MOE** = 300 (Residential, includes the FQPA SF)	Developmental Toxicity Study - rabbit LOAEL = ≤ 0.1 mg/kg/day based on: maternal toxicity of decreased body weight gain, decreased food consumption, and decreased food efficiency.
Short-Term Dermal (1-7 days) (Occupational/ Residential)	dermal study NOAEL= 5 mg/kg/day	**LOC for MOE** = 100 (Occupational) **LOC for MOE** = 100 (Residential, includes FQPA SF)	21-Day dermal toxicity study - rabbit LOAEL = 10.0 mg/kg/day based on: decreased body weight gain, and food consumption in both sexes.
Intermediate-Term Dermal (1 week - several months) (Occupational/ Residential)	dermal study NOAEL= 5 mg/kg/day	**LOC for MOE** = 100 (Occupational) **LOC for MOE** = 100 (Residential, includes FQPA SF)	21-Day dermal toxicity study - rabbit LOAEL = 10.0 mg/kg/day based on: decreased body weight gain, and food consumption in both sexes.
Long-Term Dermal (several months - lifetime) (Occupational/ Residential)	oral study NOAEL= 0.019 mg/kg/day (dermal absorption rate = 1%)	**acceptable MOE** = 100 (Occupational) **acceptable MOE** = 100 (Residential, includes FQPA SF)	Chronic/carcinogenicity study - rat LOAEL = 0.059 mg/kg/day based on: increased incidence of seizures and death, alterations in clinical chemistry (protein), increased TSH, and decreased T4.
Short-Term Inhalation (1-7 days) (Occupational/ Residential)	oral study NOAEL= 0.05 mg/kg/day (inhalation absorption rate = 100%)	**LOC for MOE** = 100 (Occupational) **LOC for MOE** = 100 (Residential, includes FQPA SF)	Developmental neurotoxicity - rat LOAEL = 0.90 mg/kg/day based on: decrease in group mean pup weights during lactation, and significant increase in time of preputial separation in males (dietary).
Intermediate-Term Inhalation (1 week - several months) (Occupational/ Residential)	oral study NOAEL= 0.05 mg/kg/day (inhalation absorption rate = 100%)	**LOC for MOE** = 100 (Occupational) **LOC for MOE** = 100 (Residential, includes FQPA SF)	Developmental neurotoxicity - rat LOAEL = 0.90 mg/kg/day based on: decrease in group mean pup weights during lactation, and significant increase in time of preputial separation in males (dietary).
Long-Term Inhalation (several months - lifetime) (Occupational/ Residential)	oral study NOAEL= 0.019 mg/kg/day (inhalation absorption rate = 100%)	**acceptable MOE** = 100 (Occupational) **acceptable MOE** = 100 (Residential, includes FQPA SF)	Chronic/carcinogenicity rat study LOAEL = 0.059 mg/kg/day based on: increased incidence of seizures and death, alterations in clinical chemistry (protein), increased TSH, and decreased T4.

Cancer (oral, dermal, inhalation)	Group C - possible human carcinogen	Use chronic RfD to estimate human risk	Increases in thyroid follicular cell tumors with fipronil (male/female)

[1] UF = uncertainty factor, FQPA SF = FQPA Safety Factor, NOAEL = no observed adverse effect level, LOAEL = lowest observed adverse effect level, PAD = population adjusted dose (a = acute, c = chronic) RfD = reference dose, LOC = level of concern, MOE = margin of exposure.

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